

Claims:

1. A method for reducing heme loss in a hemoglobin comprising altering the amino acid sequence of a subunit of the hemoglobin with a mutation that reduces heme loss, wherein said mutation is selected from the group consisting of:
 - 5 (a) adding a D-helix region to an alpha subunit of said hemoglobin;
 - (b) altering the following amino acid residues in the beta subunit of said hemoglobin: Leu28(B10), Met32(B13), Thr38(C4), Phe41(C7), Phe42(CD1), Ser44(CD3), Phe45(CD4), the entire D-helix, His63(E7), Gly64(E8) Lys66(E10), Val67(E11), Ala70(E14), Leu88(F4), Leu91(F7), His92(F8), Leu96(FG3), Val98(FG5), Asn102(G4), Phe103(G5), Leu106(G8), Leu110(G12), Gly136(H14), Val137(H15), or Leu141(H19), wherein said beta subunit amino acid residues are identified by the native beta globin amino acid sequence of human hemoglobin; and
 - 10 (c) altering the following amino acid residues in the alpha subunit of the hemoglobin: Leu29(B10), Leu31(B13), Thr39(C4), Tyr42(C7), Phe43(CD1), His45(CD3), Phe46(CD4), His58(E7), Gly59(E8), Lys61(E10), Val62(E11), Ala65(E14), Leu83(F4), Leu86(F7), His87(F8), Leu91(FG3), Val93(FG5), Asn97(G4), Phe98(G5), Leu101(G8), Leu105(G12), Ser131(H14), Val132(H15), or Leu136(H19), wherein said alpha subunit amino acid residues are identified by the native alpha globin amino acid sequence of human hemoglobin.
2. The method of claim 1, wherein said mutation is the addition of a D-helix region to the alpha subunit.
- 25 3. The method of claim 2, wherein said mutation further comprises removing the D-helix region from the beta subunit.
4. The method of claim 1, wherein said mutation is substituting an amino acid residue in the alpha or beta subunit as follows: E11->Trp, E11->Leu, B10->Phe, B10->Trp, G8->Phe, G8->Trp, CD3->His, E11->Phe, F4->Phe, H14->Leu, B10->Val or B10->Ile.
- 30 5. The method of claim 5, wherein said substitution is CD3->His in the beta subunit.
- 35 6. A mutant hemoglobin comprising mutating a beta subunit, wherein said mutation is at Thr38(C4), Phe4(C7), D-helix, Gly64(E8), or Gly136(H14).

7. A mutant hemoglobin comprising mutating an alpha subunit, wherein said mutation is at Thr39(C4), Gly59(E8) or Ser131(H14).
- 5 8. A mutant hemoglobin produced by substituting an amino acid residue in a beta or alpha subunit of a hemoglobin as follows: CD3->His, F4->Phe, H14->Leu or B10->Val.
9. The mutant hemoglobin of claim 9, wherein said substitution is
10 CD3->His in the beta subunit.

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PATENT DRAWINGS